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In re Application of

Inventor: Christopher A. Schantz et al.

Title: ARRAY FABRICATION WITH
DROP DETECTION

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Hon. Commissioner for Patents
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P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Group Art Unit: 1634

Examiner: Betty J. Forman

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Date May 12, 2003

REPLY BRIEF

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REPLY BRIEF

This is a Reply Brief in response to the Examiner's Answer mailed 03/11/02003. Applicants make the following observations with respect to Part (11) "Response to Argument" of the Answer.

In the continuing paragraph at the top of page 4, the Examiner states that "Brennan is obviously concerned with precisely controlling the droplet volume and accuracy dispensing the biopolymers" and references Column 2, lines 1-7 for this assertion. Column 2, lines 1-7 are reproduced below:

"However, existing or suggested methods are limited, and do not conveniently and reliably produce the very large, high density arrays. There is, therefore, a need for new methods for preparing large high density arrays of reactive sites. Ideally, such methods should utilized relatively simple machinery to produce large, dense arrays of solid phase bound reactants in a reproducible and rapid manner."

While the foregoing lines do indeed deal with convenience and reliability, there is no concern expressed with droplet volume and accuracy, contrary to the Examiner's suggestion. However, even if they did, this does not change the arguments in the Appeal Brief or the present Reply since such do not rely upon whether or not the foregoing lines in fact suggest what the Examiner alleges.

The Examiner's "Response to Argument" raised arguments with respect to the different claim Groups, which will be addressed below.

Groups I – Claims 4, 5, 9, 28, 29 and 43; Group IA – Claims 5, 29

The Examiner refers to Column 6, lines 23-49 of Schantz et al. for the feature of, when an error is detected, activating an operator alert and/or compensating for the error. The Examiner then goes on to state that this meets the limitation of claim 29. However, claim 29 recites as follows:

"when the error is detected the processor activates the operator alert or operates the apparatus so as to correct for the error before, or compensate for the error during, dispensing of the other droplets for that same array" (emphasis added)

This requires that there be dispensing of other droplets for the same array following correction or during compensation of the error. As discussed on page 10 of the Appeal Brief, the Examiner has not pointed to anything in the references which disclose or suggest such a feature and, if anything, the references actually teach away from such a feature. Nothing in the referenced Column 6, lines 23-49 disclose or suggest anything in relation to either of these events "for that same array". Accordingly, the reasons why the Examiner has failed to establish a *prima facie* case, as presented on Page 10 of the Appeal Brief, remain valid.

Group IB – Claim 9

Claim 9 further required:

"the dispenser unit comprises a pulse jet which ejects a droplet in response to a signal and which can de-prime, and the error is corrected by re-priming the pulse jet"

The Examiner argues that the voltage application in Schantz et al. to the ink jet, constitutes a "priming" and "re-priming" as such a voltage application "stimulates" the dispenser. The Examiner refers to the dictionary definition of "priming" presented on pages 11-12 of the Appeal Brief as including such "stimulating". In the foregoing definition, "stimulate" was definition number sixth. The first definition of "priming" is "FILL, LOAD". Furthermore, on the top of page 12 of the Appeal Brief, Applicants point out by reference to the specification (page 17, lines 7-12; page 19, lines 14-17, 21-24), as to why the "FILL, LOAD" definition would be the definition reasonably applied to "priming" in view of the specification. Furthermore, the above language of claim 9 itself refers to a pulse jet which can "de-prime" and then correcting the error by "re-priming" the pulse jet. Given the foregoing, one of ordinary skill would interpret "priming" in Claim 9 as being "FILL, LOAD". As discussed on the top of Page 12 of the Appeal Brief, the Examiner has not pointed to any suggestion for correction of an error by re-priming a pulse jet which can de-prime, and accordingly has not met her burden of establishing a *prima facie* case of obviousness.

Group II – Claim 7

As the Examiner points out, claim 7 further requires changing the biopolymer or biopolymer precursors, and performing the evaluation after the changing and before the dispensing of any droplets for an array. This can be particularly beneficial since

following changing of fluids deposited drop parameters may change (due to different fluids) or air bubbles may be trapped in the liquid (with possible deleterious effects during dispensing, such as change in volume of drops deposited).

In the Reply Brief the Examiner references various portions of Schantz et al. for the concept that the print head is being "consistently evaluated", and states that it would have been obvious to combine this with Brennan's array fabrication technology. However, nothing in the foregoing discloses or suggests specifically performing the evaluation after changing and before dispensing for an array. In fact, the only suggestion as to when one should check in Schantz et al. is at the end of a printed page 6, lines 38-42. Accordingly, as pointed out on pages 12-13 of the Appeal Brief, the Examiner has not met her burden of establishing a *prima facie* case of obviousness for the invention as claimed.

Group III – Claims 10, 11, 31, 32, 44; Group IIIA – Claims 11, 32

The Examiner comments on claim 32 in the Reply Brief. Claim 32

"the processor additionally communicates an identity of the identified defective features to a remote location or saves such information onto a storage medium"

The Examiner's argument relating to combining Brennan with Schantz et al. is summarized at the bottom of Page 8 of the Reply Brief:

"Schantz et al teach processor controlled deposit and error detection. Brennan suggests controlled deposit and accurate deposit of biopolymers is desired. It would have been obvious to one of ordinary skill to combine the teachings of Schantz et al. and Brennan and to modify the algorithm of Schantz to identify feature errors on the biopolymer array of Brennan for the obvious benefit of accurate and precise deposit of Brennan's biopolymer onto their array."

First, the Examiner refers to various portions of Brennan for a discussion on the need for depositing biopolymers with accuracy (specifically, Column 2, lines 5-7, 18-22 and Column 9, lines 55-57). While the foregoing lines do refer to oligonucleotide density and the need for machinery which will produce arrays in a "reproducible and rapid manner", nothing in the foregoing lines refers to the need for accurate deposition of drops, particularly to the point where the deposition devices themselves cannot be relied upon to produce the required accuracy for array fabrication purposes.

Second though, even assuming the correctness of the Examiner's argument above, while the Examiner alleges that it would have been obvious to modify Schantz to identify feature errors on Brennan's biopolymer array, this allegation does not amount to the required pointing to a suggestion or motivation in the references for tracking feature errors. At best, all that the suggested combination of Schantz et al. and Brennan amount to would be a suggestion that if there is a problem with the dispenser then one should provide an operator alert and/or correct the error. The Examiner has failed to point to any suggestion in the references for specifically identifying defective features, and communicating or saving such identification (nor is there any). Accordingly, the Examiner still has not satisfied her burden of establishing a *prima facie* case of obviousness.

Group IV – Claims 13, 14

Claim 13 additionally requires:

“the evaluated performance characteristic is whether one or more of the pulse jets are primed prior to dispensing any droplets for an array”

The Examiner relies upon Schantz et al. as teaching whether the jets were “fired/stimulated” prior to deposit. This argument requires equating “priming” with “firing” or “stimulating”. As discussed above, and on page 15 of the Appeal Brief, “priming” of a pulse jet refers to filling or loading. Thus, the evaluated performance characteristic is whether one or more pulse jets was in fact filled or loaded, and which is determined prior to dispensing any droplets for the array. The Examiner still has not pointed to any disclosure or suggestion in the references for evaluating whether the pulse jets were indeed “filled” or “loaded” “prior to dispensing any droplets for an array”. Accordingly, the Examiner still has not satisfied her burden of establishing a *prima facie* case of obviousness.

Group V – Claim 17

Claim 17 additionally recites:

“and wherein the sensor comprises the substrate”

The Examiner states that this is only an optional requirement apparently since the preceding phrase in claim 17 recites that the “sensing element optionally comprises the substrate”. Claim 17 as originally filed recited:

"A method according to claim: 1 wherein the sensor comprises the substrate."

Clearly that claim as originally filed required the presence of the sensor comprising the substrate. By the amendment mailed Sept. 23, 2002 the only change made to this claim 17 was to re-write it in independent form by incorporating all the limitations of claim 1. While the phrase of claim 1 "wherein the sensing element optionally comprises the substrate" is redundant in claim 17, since claim 17 always actually required the sensor to comprise the substrate no substantive change was made to claim 17 by virtue of merely re-writing it independent form. Accordingly, claim 17 still requires the sensor to comprise the substrate. As pointed out on page 16 of the Appeal Brief, the Examiner has failed to establish a *prima facie* case of obviousness by pointing to the required suggestion or motivation for this feature in the prior art. (Note that "sensor" and "sensing element" have been used interchangeably in the present application, as witnessed by original claim 17 itself and, for example, page 4, lines 3-7; page 5, lines 7-12 and 19-23.)

Group VI – Claim 6, 30

The Examiner refers to claim 30 which additionally requires:

"when the error is detected the processor operates the apparatus so as to correct for the error before, or compensate for the error during, dispensing of the other droplets for other of the arrays on the same substrate."

The Examiner references Brown et al. for a motivation to apply the error compensation of Schantz et al. to the dispensing on the same substrate. However, while Brown et al. do teach the concept of multiple arrays on the same substrate, the Examiner has not pointed to anything in Brown et al. (or Schantz et al. or Brennan) which discloses or suggests that one should correct for the error before, or compensate for the error during, dispensing of the other droplets for other of the arrays on the same substrate. Accordingly, the Examiner has not satisfied her burden of establishing a *prima facie* case of obviousness.

Group VII – Claims 15, 16; Group VIII – Claim 16

With regard to claim 16, the Examiner states that:

"It would have been obvious to modify the dispenser of Schantz et al. and Brennan with the dispenser which scans across the substrate as taught by

Brown et al. to thereby dispense repeatedly and accurately the biopolymer droplets for the expected benefit of providing a substrate capable of rapid and convenient screening as taught by Brown et al. (Column 15, lines 59-67)”

However, even assuming the correctness of this statement the claimed invention is still not obtained. Specifically claim 16 argued by the Examiner requires:

“wherein the sensing element is struck by droplets so as to generate electrical signals when the dispenser unit passes beyond the array being fabricated on each of multiple scans during fabrication of the array”

Thus, claim 16 requires striking the sensing element on each of multiple scans during fabrication of the array. The Examiner has not alleged that the references or any combination of them, discloses or suggests this feature during each of multiple scans during fabrication of the array. Accordingly, the Examiner has not satisfied her burden of establishing a *prima facie* case of obviousness of this claim.

Group IX – Claim 21

The Examiner argues:

“However, Fleischer et al. teach the motivation for evaluating performance characteristics (e.g. positioning and relative positioning of droplet dispensing i.e. proper dispensing alignment is critical for quality substrate fabrication. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to further analyze the performance of the dispenser by dispensing droplets at two or more distances from the sensor to thereby analyze numerous performance characteristics for the obvious benefits of fabricating a substrate of the highest quality.”

Claim 21 additionally requires:

“the method additionally comprising dispensing multiple droplets from the dispenser unit at each of at least two different distances from the sensor, and wherein droplet velocity is evaluated based on the phase difference between the detected signal from multiple droplets at each distance”

First, Fleischer et al. merely discloses finding drop location in a plane as illustrated in FIG. 8 (note that Fleischer et al. refers to the “horizontal” and “vertical” directions given the vertically oriented mounting configuration shown in FIG. 8). While the Examiner makes the bare allegation that it would have been obvious to further analyze the dispenser performance by dispensing droplets at two or more

distances from the sensor, the Examiner does not point to any motivation, suggestion, or reason from Fleischer et al. (or the other references) as to why one would should do this.

In addition, even if one did the Examiner points to nothing in Fleischer et al. which discloses or suggests then using the phase difference between detected signals as required by claim 21 (versus another method such as simple time of flight referenced by Fleischer et al. at Column 6, lines 27-30 in his method in which distance to a sensor is not varied).

Accordingly, for either of these foregoing reasons the Examiner has failed to satisfy her burden of establishing a *prima facie* case of obviousness for the invention as claimed.

Group X – Claim 38


Claim 38 requires:

“wherein the processor causes the dispenser unit to dispense multiple droplets at each of at least two different distances from the sensor, and wherein droplet velocity is evaluated based on the phase difference between the detected signal from multiple droplets at each distance”

The Examiner relies on the same combination of Schantz et al., Brennan, and Fleischer et al. as discussed above in connection with claim 21. As discussed above, the Examiner has not in fact pointed to any suggest or motivation from the references to deposit droplets at different distances from the sensor. Additionally, the Examiner has not pointed to then using the phase difference between detected signals (indeed, the Examiner does not even allege any suggestion or motivation from the references for using the phase difference in this context). Accordingly, for either of the foregoing reasons the Examiner has failed to satisfy her burden of establishing a *prima facie* case of obviousness.

Accordingly, for the above reasons and the reasons discussed in the Appeal Brief, all of the rejections of claims 4-7, 9-11, 13-17, 21, 28-32, 38, 43, 44, should be reversed.

Respectfully submitted,



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